Frontiers in Mechanochemistry and Mechanical Alloying

INCOME2008
1-4 December, 2008

APPLIED MECHANOCHEMISTRY OF SOLIDS (A REVIEW)

Peter Baláž[ξ], Erika Dutková
Institute of Geotechnics, Slovak Academy of Sciences, Watsonova 45, 043 53 Košice, Slovakia

Keywords: Mechanochemistry, Applications, Solids

Abstract

This review paper deals with the application of broad possibilities of mechanochemistry in mineral processing, extractive metallurgy, chemical engineering, building industry, coal industry, materials engineering, agriculture, pharmacy and waste treatment. In several applications pilot plants units or full commercial units were successfully applied. The environmental aspects of these processes are particularly attractive. The main advantages in comparison with traditional technological procedures are decrease in number of technological stages, exclusion of operations that involve the use of solvents and gases and last but not the least the possibility obtaining a product in the metastable state which is difficult to obtain using traditional technological methods. There is a great potential of mechanochemistry in technology and several examples with a possibility for industrial applications are given.

Introduction

Mechanical activation by means of ultrafine milling is an effective procedure where an improvement in technological processes can be attained via a combination of several effects which influence the properties of applied solids. The main advantages in comparison with the traditional technological procedures are decrease in the number of technological stages, excluding the operations that involve the use of solvents and gases and the possibility of obtaining a product in the metastable state which is difficult (or impossible) to obtain using traditional technological methods [1]. Nanoparticles are often formed by this technological approach which adds value to the processed solids [2]. The environmental aspects of these processes are particularly attractive [3].

Extractive Metallurgy

According to classical view extractive metallurgy is the art and science of extracting metals from their ores by chemical methods [4]. It is actually divided into three sectors: hydrometallurgy, pyrometallurgy and electrometallurgy. Hydrometallurgy is the technology of extracting metals from ores by aqueous methods, pyrometallurgy by dry thermal methods, and electrometallurgy by electrolytic methods.

In general, hydrometallurgy involves two distinct steps (Fig. 1): selective dissolution of the metal values from an ore – process known as *leaching* and selective recovery of the metal values from the solution, an operation that involves a *precipitation* method. Sometimes a purification/concentration operation is conducted prior to precipitation. These processes are aimed at obtaining a pure and a concentrated solution from which the metals values can be precipitated effectively. The methods used are: adsorption on activated charcoal, sorption on ion exchange resins, extraction by organic solvents as well as other advanced processes of metals extraction [5]. Selected examples of the applications of mechanical activation in extractive metallurgy are given in following paragraphs.

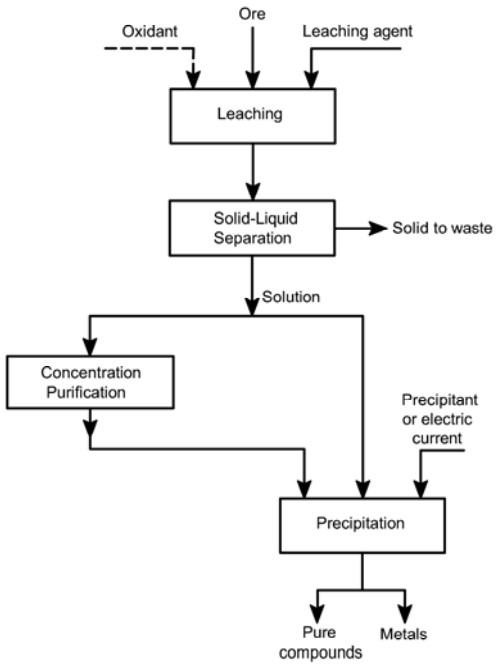


Figure 1. General outline of hydrometallurgical process [4]

Gold and Silver

The technologies hitherto used encounter a problem in processing complex sulphide ores containing gold and silver in an economic way providing sufficient recovery. One of the problems of gold and silver extraction from sulfidic minerals is associated with the form in which the precious metals occur.

Gold and silver are frequently physically-locked within sulphides, may form defects in their structure or can be chemically bonded in the form of solid solutions or compounds [6-8]. Different types of associations of gold with sulphidic minerals are given in Fig. 2.

[ξ] email : balaz@saske.sk

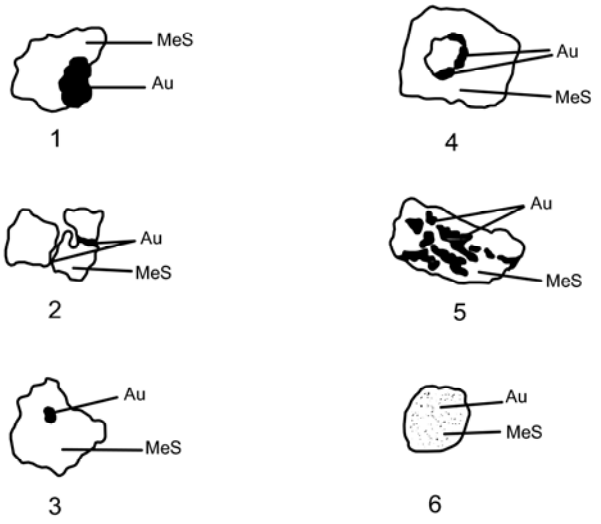


Fig. 2 Gold associations with sulphide minerals: 1-readily liberatable gold, 2-gold along crystal grain boundaries, 3-gold grain enclosed in pyrite/sulfide (random position), 4-gold occurrence at the boundary between sulfide grains, 5-gold in concretionary pyrite (or other sulfide) along fractures and/or crystal defects, 6-gold as colloidal particles or in solid solution in sulfide [7-8].

Sulphides are also a considerable natural resource of silver. Around 200 minerals bearing silver in major, minor and variable amounts have been detected [9]. However, of these, only 10-12 minerals are of practical importance. These are, in order of leachability: elemental silver, silver halides and silver sulfides [10].

The contact of gold and silver (in form of metals or compounds) with leaching reagent plays a fundamental role in the hydrometallurgical extraction of the precious metals. An improvement of the contact can be achieved by the pretreatment. The choice of pretreatment method significantly depends on locality and mineralogy of the ore deposit. The oxidizing pretreatment, which can, in principle, proceed in the pyrometallurgical or hydrometallurgical way, belongs among classical methods [7]. Pyrometallurgical pretreatment is the oldest application and consists of an oxidizing roast to convert sulfides to oxides. However, because of environmental demands roasting is becoming more and more suppressed, irrespective of technical innovations [11].

Chemical and biological pretreatments are applied in hydrometallurgical processes, the goal of these processes is to disintegrate the sulphide and thus to facilitate the subsequent extraction of gold and silver. Pressure oxidation can be used for this but has high capital and operating costs. At present, one of the increasingly used processes is biological oxidation, this is considered acceptable from the view-point of environmental considerations and lower economic demands (see Table 1). However, long reaction times and appropriate design of bioreactors often create difficulties.

Table 1. Relative costs of pretreatment processes [12].

Pretreatment	Costs	
	Capital	Operating
Roasting	1.0-1.5	0.75-0.80
Pressure oxidation	1.20-1.25	0.90-0.95
Biological oxidation	1.0	1.0

The process of fine and ultra-fine milling for pretreating gold and silver contentrates has been used very often in recent years. This process requires finer milling than that attained in the ball mills typically used in comminution for flotation. Particle size of 1-20 μm can be produced in intensive milling where size reduction is accompanied by mechanical activation of mineral components.

The effect of combination of fine milling in ball mill, classification and mechanical activation in attritor on gold and silver recovery from a chalcopyrite concentrate has been studied [13]. The proposed flowsheet is in Fig. 3.

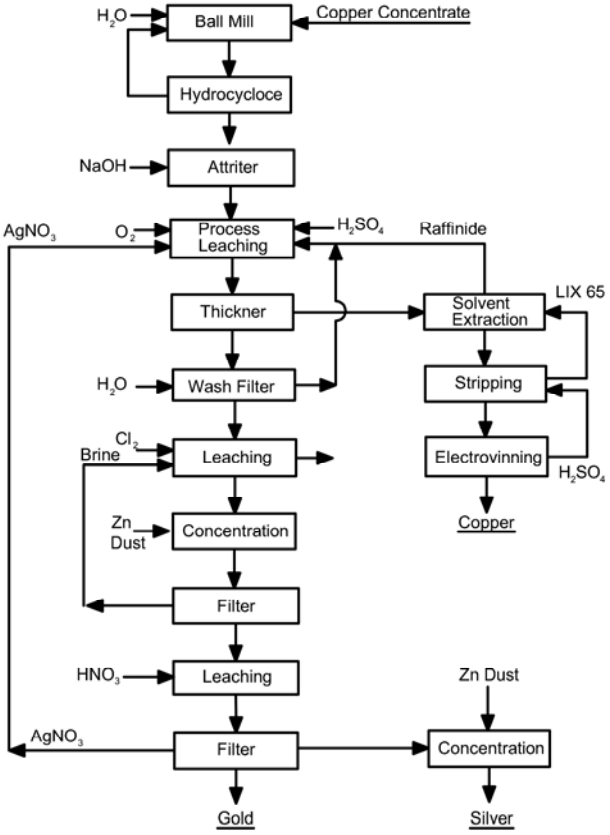


Figure 3. Flowsheet for the treatment of chalcopyrite concentrate by attrition and acid pressure leaching with catalyst ($AgNO_3$) including recovery of Ag and Au [13].

The processing of sulfidic concentrate (5-6% $CuFeS_2$, 53-55% FeS_2, 8-10% FeAsS) has been studied by the following strategy: two-step cyanidation-mechanical activation-air conditioning-cyanidation [14]. The proposed flowsheet is in Figure 4 and conditions are given in Table 2.

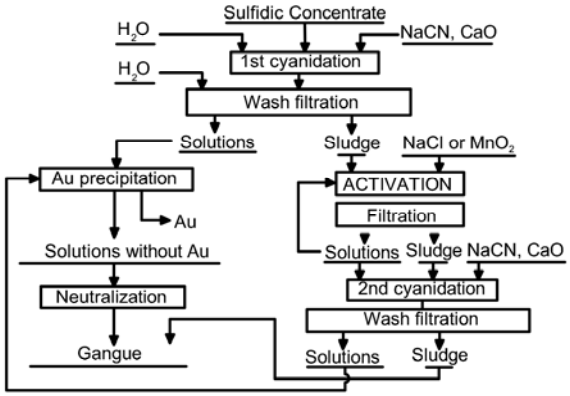


Figure 4. Flowsheet for the treatment of sulfidic concentrate by vibration milling for gold recovery [14].

Table 2. Results of gold extraction from cyanidation of sulfidic concentrate [14].

Parameter	Mechanical activation		
	in NaCl solution (60 gl^{-1})	with MnO_2 addition (1%)	
Revolutions of the planetary mill (min^{-1})	800	800	600
Au in solid rest after 1st cyanidation (gt^{-1})	9.8	9.4	9.4
Cyanidation after 1st activation and pulp aeration			
NaCN (gl^{-1})	0.7	0.4	0.3
Leaching time (h)	19	18	16
Au in solid rest (gt^{-1})	4.4-6.0	3.6-5.0	4.6-5.0
Cyanidation after 2nd activation and pulp aeration			
NaCN (gl^{-1})	0.3	0.5	0.5
Leaching time (h)	22	18	26
Au in solid rest (gt^{-1})	3.4-3.8	3.0-4.0	3.2-4.0
Au recovery (%)	93.5	93.7	93.5

Chromium

Chromite $FeCr_2O_4$ is the source mineral for the production of chromium metal, ferrochromium, special alloys and Cr chemicals. The annual worldwide production of chromium chemicals is estimated to be approx. 1 million tons, as sodium dichromate $Na_2Cr_2O_7$ [15]. The only relevant process for production of chromates is the oxidative digestion of chromites using Na_2CO_3 at 1000-1100°C. In order to prevent the melt from sticking, a leaning agent such as $CaCO_3$ is added to the digestion mixture, to give the melt a loose structure and to facilitate the diffusion of the oxygen to the chromite. The process is governed by reactions

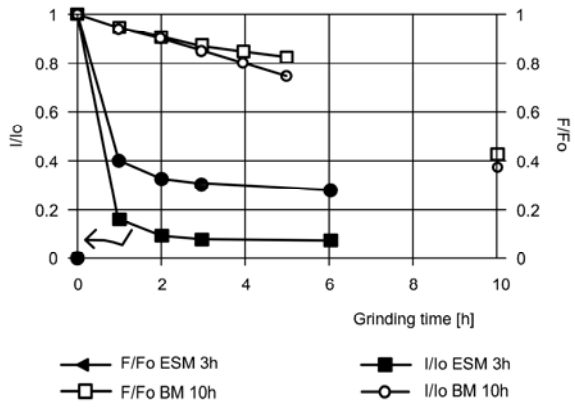
$$FeCr_2O_4 + 4Na_2CO_3 + 4CaO + 7O_2 \rightarrow 4Na_2CrO_4 + 4CaCrO_4 + 2Fe_2O_3 + CO_2 \quad (1)$$

$$2Na_2CrO_4 + 4CO_2 + H_2O \Leftrightarrow Na_2Cr_2O_7 + 2NaHCO_3 \quad (2)$$

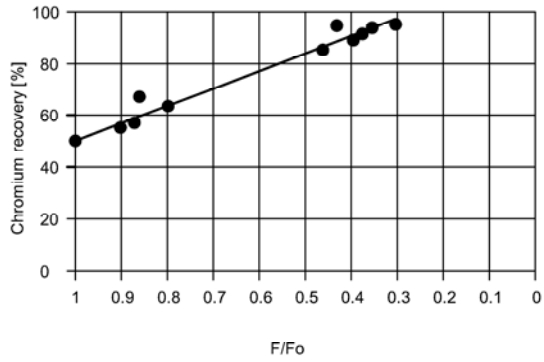
Calcium chromate $CaCrO_4$, as opposed to sodium chromate Na_2CrO_4 is poorly soluble, so that the recovery of chromate may be impaired during the leaching of the digestion cake. $Na_2Cr_2O_7$ is won as a crystallizate and is the source material for the production of most chromium compounds.

The disadvantage of the above-described process is that it is impossible to achieve a complete digestion of the chromite ores. Mechanical activation as pretreatment step to improve the digestion step has been applied [16].

Two types of mills were used for comparison, a laboratory scale ball mill (BM) and an industrial eccentric vibratory mill (ESM).



(a)



(b)

Figure 5. (a) Relative X-ray intensities I/I_0 and F/F_0 for lattice plane (311) of chromite $FeCr_2O_4$ for BM and ESM milling and (b) chromium recovery after digestion of chromite vs. F/F_0 ratio [16].

In Figure 6 the modified flowsheet for the production of sodium dichromate is given. The introduction of mechanical activation step enabled the reduction of the mass flows due to a complete digestion and the improved landfill-suitability of the tailings.

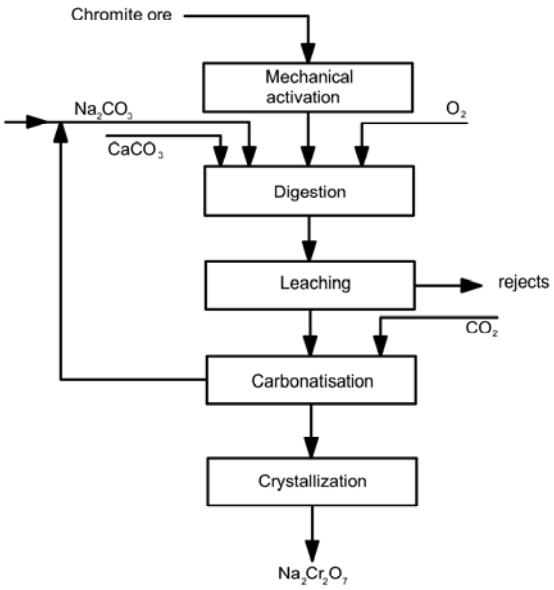


Figure 6. Flowsheet for sodium dichromate $Na_2Cr_2O_7$ production with introduction of mechanical activation step [16].

Aluminium

Investigations were performed in Germany in order to elucidate possibilities to improve processing steps of the hydrometallurgical treatment of bauxite ores by the Bayer process with mechanochemical method [17-19].

Bauxite $Al(OH)_3$ is usually a composition of three minerals: hydrargillit (α-$Al(OH)_3$), böhmit (γ-AlO(OH)) and diaspor (α-AlO(OH)) with various leachability. The use of NaOH to leach bauxite was invented by Bayer in 1892 as a process for obtaining pure aluminium hydroxide which can be calcinated to pure Al_2O_3 suitable for processing to metal [4]. About 2 tons bauxite yield 1 ton Al_2O_3 from which 0.5 ton aluminium is produced.
The reactions in NaOH leaching are the following

$$Al(OH)_3 + OH^- \rightarrow [AlO(OH)_2]^- + H_2O \quad (3)$$

$$AlO(OH) + OH^- + H_2O \rightarrow [AlO(OH)_2]^- \quad (4)$$

Tests in an attritor revealed that the pressure leaching extraction of the aluminium hydroxides in the bauxite by sodium hydroxide solutions could already be achieved with high extraction rates at 90°C after relatively short treatment times. Additional favourable results indicate that CaO additions to the bauxite are effective to avoid undersirable sodium silicate formation in the sodium aluminate solution and that the black residual sludge contains up to 70% hematite Fe_2O_3 and nearly negligible aluminium and sodium amounts which might allow to consider further applications which could avoid disposal problems encountered with the conventional red mud precipitates [18, 19-20]. The comparison of the Bayer process and the mechanochemical processes is given in Table 3.

Table 3. Comparison of the Bayer and mechanochemical processes [18].

Parameters	Bayer process	Mechanochemical process
Wet milling to (-200μm)	+	+
SiO_2 removal	+	-
Chemical decomposition	250°C, 100 bar	90°C, 1 bar
Na_2O content in leaching medium	140 gL^{-1}	250 gL^{-1}
Maximum content of Al_2O_3 in leaching solution	185 gL^{-1}	300 gL^{-1}
Residence time	3 min	15 min
Thickener	+	+
Filtration	+	+
Rest	2 t red mud/t Al_2O_3	0.75 t black mud/t Al_2O_3
Cooling to 50°C	+	+
Colour of leaching solution	Brown	colourless
Addition of inoculation substance	300 gL^{-1}	-
Conditioning	50 h	4 h
Filtration	+	+
Filtrate to disposal	+	+

Copper, Nickel and Cobalt

During the International Conference Copper Cobre 2003 in Chile the status of copper hydrometallurgy and the most commercially attractive potential applications were reviewed [21]. The main processes applying sulfate leaching are listed in Table 4.

Amongst them, Activox and Nenatech processes apply fine milling. The particle size of concentrate into leaching is usually less than 20 microns. The features of these processes include

- leaching temperature in these process is lower than sulfur melting temperature (119°C)
- element sulfur formed in the processes remains in the leaching residue which leads to the difficulty to recover precious metals from leaching residue
- some sulfate is produced that is precipitated as gypsum
- iron precipitation is as goethite and jarosite

The Activox process was developed in Australia as an alternative to the pretreatments of sulfidic concentrates by roasting and bacterial oxidation [22-28]. The process has been applied to the recovery of non-ferrous and precious metals from concentrates and calcines. A principle idea of Activox is shown in Fig. 7.

Table 4. New sulfate processes for chalcopyrite concentrate leaching [21].

Process	Leach pressure	Sulfur product	Proposed mechanism	Level of development	Note
Activox	Low	S^o SO_4^{2-}	Direct	Laboratory	1*
Nena-tech	Atmos-pheric	S^o SO_4^{2-}	Direct	Laboratory	1
Dyna-tec	Pressure (medium)	S^o	Direct	Laboratory	2
AAC/ UBC	Pressure (medium)	S^o	Direct	Pilot plant (planed)	3
Placer Dome	Pressure (high)	SO_4^{2-}	Direct	Demo plant (started 2003)	4
Biocop	Atmos-pheric	SO_4^{2-}	Indirect	Commercial (underway)	5
Bactech /Mintek	Atmos-pheric	S^o SO_4^{2-}	Indirect	Demo plant	5
Geocoat	Atmos-pheric	SO_4^{2-}	Indirect	Pilot plant	5

* Note : 1 – Fine milling; 2 – With coal; 3 – With surfactant; 4 – High temperature; 5 – Bacterial

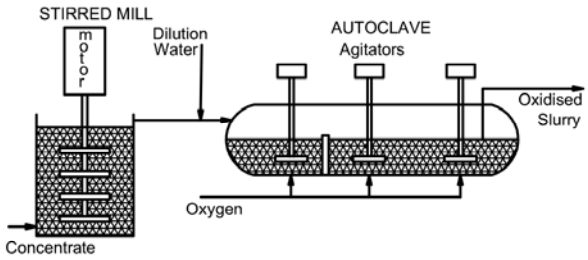


Figure 7. Activox process [26].

Activox is a hydrometallurgical process combining ultra fine milling to a P_{80} of ~10 μm with a low temperature (100°C), low pressure (1000 kPa) oxidative leach to liberate metals from a sulfide matrix. Base metals, (i.e. copper, zinc, nickel and cobalt) are extracted into the leach liquor, while gold and silver remain in the leach residue in a form suitable for further processing. The Activox conditions favour the formation of elemental sulfur over sulfate, thereby using less oxygen (usually less than 1.5 kg of O_2 per kg of S) than required for complete oxidation to sulfate (typically 2.2 kg O_2 per kg S). Other features include rapid oxidation times (1-2 hours), clean pregnant liquors, and the possibility to treat environmentally hazardous species such as arsenopyrite to produce stable ferric arsenate residues [29].

The Activox based flowsheet for the production of Ni, Co and Cu from sulfide concentrates is shown in Figure 8. The flowsheet is based on proven unit operations and only uses readily available commercial reagents. The flowsheet can handle a wide range of feed materials and is not sensitive to short or long term variations in feed grades [30].

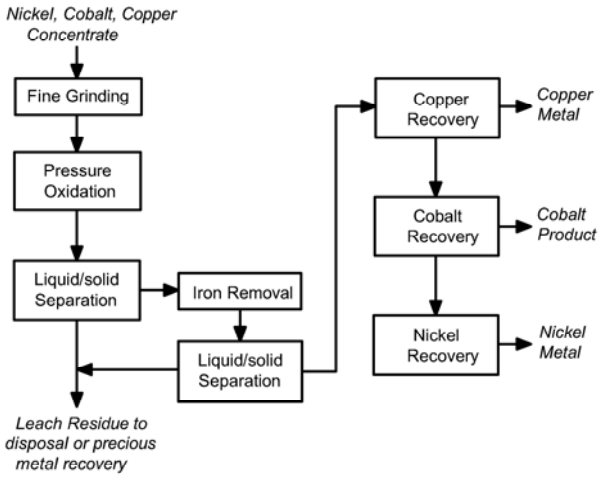


Figure 8. Flowsheet of the Activox process for production of Ni, Co and Cu [28].

As for activation equipments, three different mills including Bradkeen-Metprotech, Netzsch-IsaMill and Metso-Mineral were tested [28, 31]. IsaMill and conditions of its application are given in Fig. 9 and Table 5, respectively.

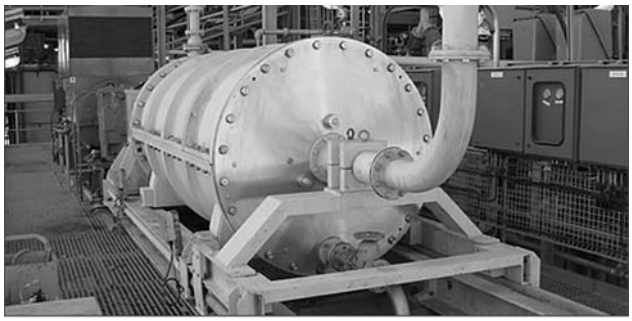


Figure 9. The horizontal stirred mill-IsaMill [32].

Table 5. Operating conditions and specific energy consumption for IsaMill [33]

Site	Mill pressure (kPa)	% Solid (by weight)	Temp-erature of exciting pulp (°C)	Size reduction ratio	Specific energy[3] ($kWht^{-1}$)
Mount Isa	225	40	40-43[2]	1.67	7.6
McArthurRiver					
-open circuit	300[1]	20	40-50[2]	3.75	28
-close circuit	425	20	40-50[2]	4.30	36

[1]Approximate value
[2]Depending on ambient temperature
[3]Based on net power draw (gross power-no load power)

Antimony

The Melt process was developed in Slovakia for hydrometallurgical treatment of tetrahedrite sulfidic concentrates in order to obtain antimony in soluble form and copper as copper sulphide [34-36]. The process name is an abbreviation: mechanochemical leaching of tetrahedrites.

Tetrahedrite is one of the most common sulfominerals. The general formula representing the naturally occurring tetrahedrite-tennantite series is $(Cu,Ag)_{10}(Cu,Zn,Fe,Cd,Hg,Cu)_2(Sb,Bi,As)_4S_{13}$. In most natural tetrahedrites the two Cu^{2+} atoms are replaced by a divalent element such as Zn^{2+} which usually occupies a tetrahedral site in sulfides [37]. Tetrahedrites represent the most important source of copper and antimony and are also of economical interest due to their content of silver and mercury.

The chemistry of the reaction between tetrahedrite (simplified formula Cu_3SbS_3) and Na_2S can be described by the following equations [38]

$$2Cu_3SbS_3 + Na_2S \rightarrow 3Cu_2S + 2\ NaSbS_2 \quad (5)$$

$$NaSbS_3 + Na_2S \rightarrow Na_3SbS_3 \quad (6)$$

The soluble Na_3SbS_3 containing trivalent antimony is oxidized to a product containing pentavalent antimony by the polysulfide ions present in the leaching liquor

$$(x\text{-}1)\ Na_3SbS_3 + Na_2S_x \rightarrow (x\text{-}1)\ Na_3SbS_4 + Na_2S \quad (7)$$

The behaviour of arsenic leaching from tennantite Cu_3AsS_3 by Na_2S may be described by the equation

$$2Cu_3AsS_3 + 3\ S^{2-} \rightarrow 3\ Cu_2S + 2AsS_3^{3-} \quad (8)$$

The principal flowsheet of operation, in which mechanochemical (I) leaching is followed by chemical (II) leaching, is shown in Figure 10. Alkaline solutions of Na_2S have been explored as leaching agent. The results presented in Table 6 show that almost total extraction of Sb can be achieved by alkaline Na_2S leaching at 95°C leaving 0.25 % Sb in solid residue.

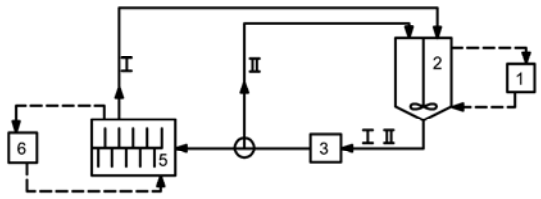


Figure. 10 Flowsheet of leaching unit: 1-heating, 2-chemical reactor, 3-pump, 4-valve, 5-attritor, 6-cooling. The working regimes: I-mechanochemical leaching, II chemical leaching [39].

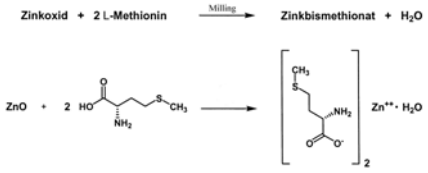
Table 6. Chemical composition of tetrahedrite concentrate [40].

Element	Me (%)	
	As received	Mechanochemically treated
Cu	27.36	26.00
Sb	15.93	0.25
Fe	14.58	16.46
Bi	0.33	0.33
As	1.02	0.27
Hg	0.74	0.11

Crystal Engineering

Mechanochemical solid-state reaction of molecular crystals is a rather new but promising direction in application of ultrafine milling. The potential importance of this field relates not solely to the traditional fields of applications of molecular crystals, such as pharmaceutics (see later) but also to the newly discovered possibilities of their utilization as functional materials for molecular electronics, molecular magnets, etc. [2].

Useful contributions into recent literature of organic solid-state reactions, including those activated mechanochemically have been published [41-43]. Various mills were tested for activation, especially those providing the high energy input such as vibratory mills, planetary mills and attritors. It was established that many types of organic reactions can be realized with these devices.
As an example, mechanochemical synthesis of zinc bismethionate, a food additive can be illustrated (Fig. 11). This compound is prepared by solid-state synthesis at ambient conditions without intervening liquid phase and connected operations like heating, washing, destilation, etc.



(9)

Figure. 11 Mechanochemical synthesis of zinc bismethionate hydrate: chemistry and milling in an industrial eccentric vibration mill ESM (Siebtechnik, Germany) [44].

Materials Engineering

Non-equilibrium processing of materials has attracted the attention of a number of scientists and engineers due to the possibility of producing better and improved materials than is possible by conventional methods [45]. One of the processing methods cited in literature under the term mechanical alloying (MA) is very frequently used for the preparation of advanced materials in materials engineering. MA started as an industrial necessity to produce oxide dispersion strengthened (ODS) nickel- and iron-based superalloys for applications in the aerospace industry [46]. The technique of MA was used for industrial applications from the beginning and the basic understanding and mechanism of the process is beginning to be understood only now. One of the greatest advances of MA is in the synthesis of novel alloys, e.g. alloying of normally immiscible elements, which is not possible by any other technique. The MA products find applications in various industries and these are summarized in Fig. 12.

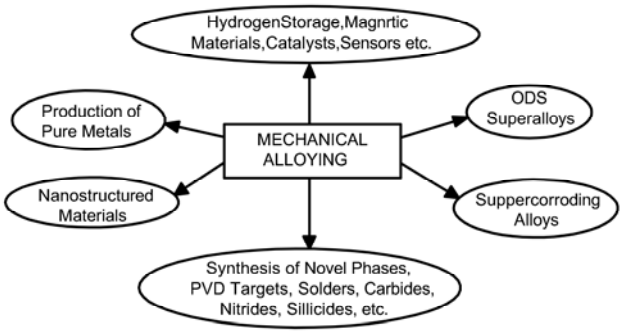


Figure 12. Typical current and potential applications of MA products [47].

Mechanical alloying for commercial production is carried out in the mills of up to more than 1000 kg capacity. The ball mills to produce oxide dispersion strengthened nickel- and iron-based alloys, is carried at facilities in the USA and Great Britain (Fig. 13).

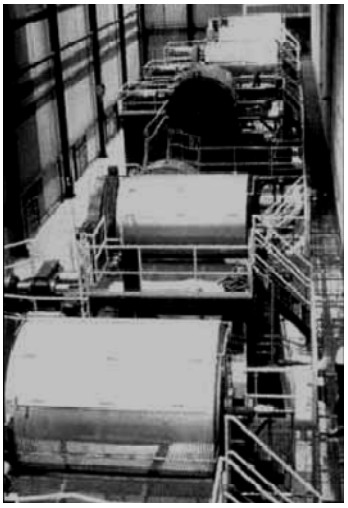


Figure 13. Commercial production-size ball mills used for mechanical alloys [47]

Agriculture

Phosphates that occur in volcanic rocks as apatites or in sedimentary rocks as phosporites are used in agriculture for production of phosphate fertilizers. Natural phosphates have first to be converted to the water-soluble form by their decomposition in acids. Superphosphate is a classical phosphorus fertilizer, produced by decomposition of phosphates in sulphuric acid. A higher grade of superphosphate with 2-3 times higher content of water-soluble phosphatic component can be prepared by decomposition of phosphates in a mixture of sulphuric and phosphoric acids [48]. Traditionally, the following reactions are used:

$$Ca_3F(PO_4)_3 + 5H_2SO_4 + 2.5H_2O \rightarrow 5(CaSO_4.0.5H_2O) + 3HPO_4 + HF \quad (10)$$

$$Ca_3F(PO_4)_3 + 7H_3PO_4 + 5\,H_2O \rightarrow 5[Ca(H_2PO_4).H_2O] + HF \quad (11)$$

Acid soils may be fertilized by natural phosphates in the as-milled state. In view of their low immediate effect, they are used as long-term fertilizers. In an attempt to enhance the efficiency extensive research to increase the fertilizing effect has been carried out [see references in works 49; 48].

Based on the results of investigation of the structure-reactivity correlation, commercial phosphate fertilizers have been developed. In Figure 14 practical application of mechanically activated Marocco phosphorite for plants treatment is shown. The positive influence of high-energy milling on plant growth is unambigous.

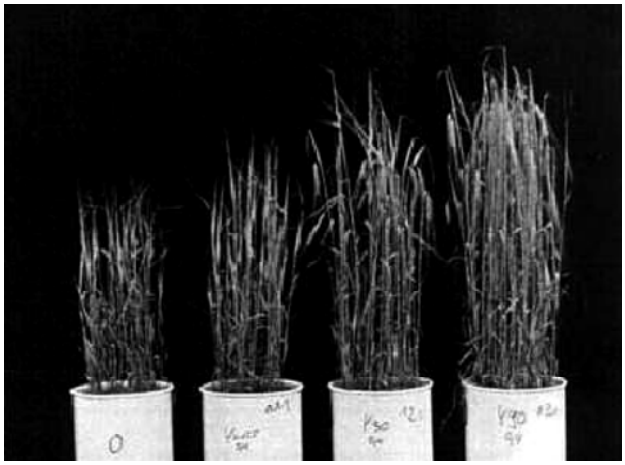


Figure 14. Influence of mechanical activation of phosphorite (deposit Youssoufia, Morocco) on a plantgrowth. From left to the right: without phosphorite, non-activated phosphorite (-125 μm), phosphorite milled at milling energy 50 kWh/t and 150kWh/t, respectively [50].

Optimal parameters of mechanical activation have been determined for the phosphate ores of different mineral compositions [51]. The mills of continuous operation with low energy consumption have been designed, their productive capacity being, at the beginning, 3t/h. Long-term agrochemical tests (for 15 years) of mechanically activated phosphate ores of different compositions have been carried out on wide range of soils and

with various crops. These tests demonstrated high fertilizing effect [52-53]. The technology was installed at the Burenkhan deposit of phosphorite ores in Mongolia. It was proved that the mechanochemicaly pretreated phosporite fertilizers have prolonged action and are comparable with fertilizer based on superphosphate [54].

The technological advantages of mechanochemical methods over traditional methods are summarized in Table 7.

Table 7. Comparison of traditional and mechanochemical methods for production of phosphate fertilizers [55].

Process characteristics	Traditional method	Mechanochemical method
Pittrman's probe in % citric acid S	80-85	55-60
Ammonium citrate	60	40-50
Increase of harvest related to superphosphate	1.00	0.95
Duration of production process	20 d (periodical)	20-24 h (continuous)
Consumption of energy per ton	450 kWh/t	500 kWh/t
Consumption of reagents per ton	0.7 t H_2SO_4 (60%)	-
Duration of agrochemical action of the fertilizer	1-2 years	5-7 years
Release of fluorine into atmosphere	Yes	No
Increase of acidity of soils	Yes	No
Possibility to use in small deposits (<1 million tons) of phosphorus rocks	No	Yes

Different machines consume different amounts of power for production of the fertilizers, and the capacity of the mills is also different. It was reported that the vibrocentrifuge mill was the best suited for this purpose and it could also be used continuously. As mentioned above, the first factory to produce the phosphate fertilizer was built in Mongolia. Since then more than 1.5 million tons of the fertilizer has been produced.

Pharmacy

Dissolution testing of drug compounds is of fundamental importance in the design and development of pharmaceutical products [56]. Dissolution rate is normally described by Noyes-Whitney equation

$$\frac{dW}{dt} = \frac{D}{h_D} S_A (C_s - C_t) \quad (12)$$

where the dissolution rate (dW/dt) at time t is a function of three types of material and experimental parameters, namely specific surface area S_A, concentration gradient (c_s-c_t) and diffusional transport D/h_D (D-diffusion coefficient, h_D-the distance over which diffusion is the dominant transport mechanism).

At present about 40% of the drugs being in the development pipelines are poorly soluble, even up to 60% of compounds coming directly from synthesis are poorly soluble [57]. Poor solubility is in most cases associated with poor bioavailability. Bioavailability is how well a drug will reach an effective therapeutical level in the body, and may be influenced by various factors. A drug may be safe and effective, but never reach the therapeutic level in the body if the bioavailability is poor. Bioavailability essentially depends on three factors: solubility, permeability and dose [58], and the question of the minimum acceptable solubility can only be answered if the other two factors are known. According to biopharmaceutics classification system a drug substance is considered highly soluble when the highest strength dosage is soluble in 250 mL of aqueous media over the range pH=1.0-7.5 [59].

There are two basic approaches to overcome the bioavailability problems of the drugs:

- increase of equilibrium solubility (e.g. by complex formation) and
- increase of dissolution velocity

The first approach was a limited success as clearly demonstrated by the low number of products on the market based on such technologies. A much more straight forward way is increasing the dissolution velocity by increasing the surface area of the drug powder, i.e. micronisation leading to mean particle sizes approximately 3-5 μm. However, many of the new compounds show such a low solubility that micronisation does not lead to a sufficient increase in bioavailability after oral administration. Therefore the next step taken was nanonization. The drug powder is transferred to drug nanocrystals, typically sizes are around 200-600 nm [60].

Drug nanocrystals can be produced by various methods principally the top down and bottom up techniques (Fig. 15).

The bottom up technique is the classical precipitation approach, the drug is dissolved in a solvent which is subsequently added to a nonosolvent to precipitate the crystals. A priori this technique is difficult to handle, the crystal growth needs to be stopped to avoid formation of microcrystals. In addition this technology cannot be applied to the increasing number of drugs being poorly soluble in all media [60]. On the other hand the top down technique (ultrafine milling) is the method of choice for industrial production in pharmacy. In addition to size reduction, milling may alter the crystalline structure and cause chemical changes in some drugs [62-63].

The advantages of mechanochemical approach applying the ultrafine milling can be illustrated for acetylsalicylic acid production.

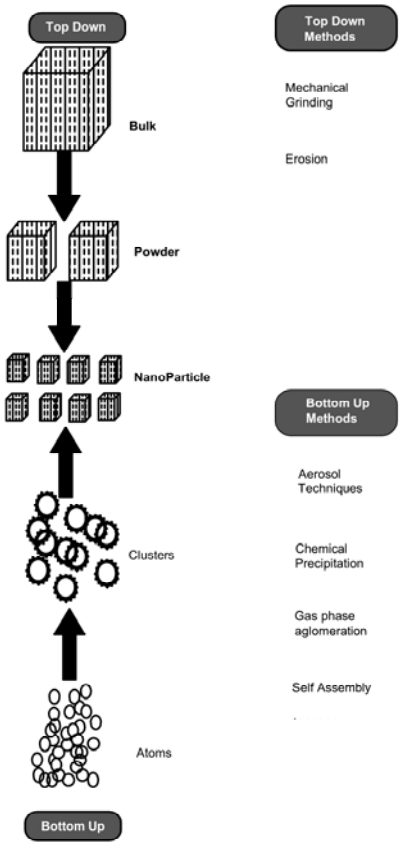


Figure 15. Schematic representation of the top down and bottom up techniques for drug nanocrystals preparation [61].

Acetylsalicylic acid (ASA) is non-steroidal substance often used as an analgesic, antipyretic and as an anti-inflammatory drug. The most popular and used brand name is Aspirin. It has also antiplatelet effect and is used in long-term, low doses to prevent heart attach and cancer. Its solubility in water is 1mg/mL at 20°C. The low solubility of ASA in water decreases its pharmacological efficiency and causes undesirable side effects when the substance is used in drugs. The salts of ASA posses increased solubility. However, with all advantages of ASA salts, these are expensive drugs manufactured on a small scale. During the production, ASA undergoes partial decomposition into salicylic and acetic acid as a result of hydrolysis. The existing requirements to the purity of the product make the production process more complex and the product more expensive [64].

For mechanochemical technology for obtaining soluble materials based on ASA and their subsequent use as drugs the special vibrocentrifugal mills with productivity 10g/h-1t/h have been designed. In order to obtain especially pure products (for pharmaceutical purposes), the inner surface of the drum and the surface of milling bodies can be coated with an inert material. The schematic diagram and a pilot plant unit is given in Fig. 16. The design allows smooth variations of the feeder productivity and mill rate. The technological regulations for production of fast-dissolved substance (brand names Aspinat and later Askopirin) have been developed and coordinated with the Ministry of Health in Russia [64].

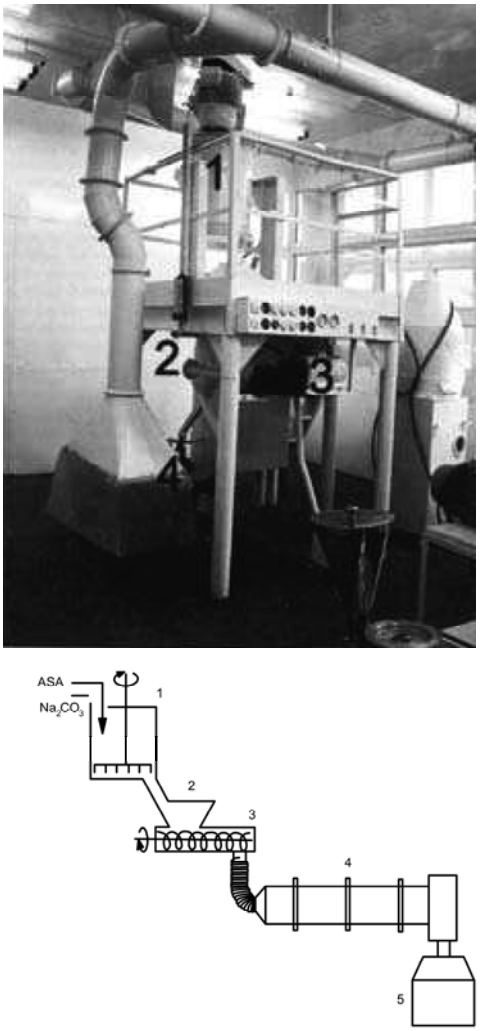


Fig. 16 Schematic diagram (bottm) and a mechanochemical pilot plant unit (top) for the production of fast-dissolving substances of ASA, 1-turbo mixer, 2,3-accumulating tank with feeding screen, 4-continuous vibrocentrifugal mill, 5-product collector [64-65].

Conclusions

The possibilities of ultrafine milling applications in extractive metallurgy, materials engineering, agriculture and pharmacy are briefly described in this paper. Mechanochemistry which applies this type of milling, demonstrates the differences in comparison with traditional technological procedures. The main advantage is decrease in the number of technological stages, exclusion the operations that involve the use of solvents and gases and the possibility of obtaining a product in the metastable state which is difficult to obtain using traditional technological procedures. The environmental aspects of these processes are particularly attractive.

Acknowledgements

The support through the Slovak Research and Developing Agency APVV (projects VV-0189-10,LPP-0107-09) and the Slovak Grant Agency VEGA (project 2/0009/11) is gratefully acknowledged.

References

1. V.V. Boldyrev, *Russian Chemical Reviews*, 75 (2006) 177.
2. P. Baláž, *Mechanochemistry in Nanoscience and Minerals Engineering,* Springer, Heidelberg, (2008)
3. O.I. Lomovskij and V.V. Boldyrev, *Mechanochemistry for Solving Environmental Problems.* GPNTB SO RAN, Novosibirsk, (2006) (in Russian).
4. F. Habashi, *A Textbook of Hydrometallurgy,* Metallurgie Extractive Quebec, Sainte Foy, Quebec, (1993).
5. T. Havlík, *Hydrometallurgy: Principles and Applications,* CRC Press, Oxford, (2008).
6. L. Lorentzen and J.S.L. van Deventer, *Hydrometallurgy*, 30 (1992) 177.
7. J. Marsden and I. House, *The Chemistry of Gold Extraction,* Ellis Horwood, New York, (1992).
8. J.B. Hiskey and V.P. Atluri, *Mineral Processing and Extractive Metallurgy Reviews*, 4 (1988) 95.
9. C. Gasparrini, *Gold and Other Precious Metals, from Ore to Market,* The Space Eagle Publishing, Tucson, (1995).
10. D.M. Wyslouzil and R.S. Salter, *Proc. Int. Symp. "Lead-Zinc'90",* (eds.) T.S. Makey, R.D. Prengaman, TMS Meeting, (1990) p. 87.
11. S.R. La Brooy, H.G. Linge and G.S. Walker, *Minerals Engineering*, 7 (1994) 1213.
12. N.C. Wall and D. Pattison, *Minerals International*, March (1997) 16.
13. F. Pawlek, *Proc. Int. Symp. Extractive Metallurgy of Copper*, Vol. II, (eds.) J.C. Yannopoulos, J.C. Agarwall, Metallurgical Society AIME, Las Vegas, (1976) p. 690.
14. V.G. Kulebakin, O.G. Terechova, V.I. Molčanov and A.M. Žižajev, *Activation of Raw Materials.* Nauka, Novosibirsk, (1999) (in Russian).
15. H.P. Münster, *Taschenbuch des Metallhandels*, Hüthig BmbH, Heidelberg, (1997).
16. H. Dincer, G. Önal and E. Gock, *Proc. Int. Miner. Process. Conf. "Mineral Processing on the Verge of the 21st Century"*, (eds.) G. Özbayoglu, C. Hostin, M.Ü. Ataloy, C. Hicyilmaz, A.I. Arol , Istanbul, Balkema, Rotterdam, (2000) p. 47.
17. E.V. Szanto and W. Schultes, *Erzmetall*, 22 (1969) 465.
18. F. Pawlek, M.J. Kheiri and R. Kammel, *Metall*, 46 (1992) 575.
19. R. Schrader and B. Hoffmann, *Festkörperchemie*, VEB Deutscher Verlag für Grundstoffindustrie, (eds.) V. Boldyrev and K. Meyer, Leipzig, (1993) p. 522-543.
20. R. Kumar, T.C. Alex, Z.H. Khan, S.P. Mahapatra and S.P. Mehrotra, *Proc. Int. Conf. "Light Metals 2005"*, (ed.) H. Kvande, The Minerals, Metals & Materials Society, Warendale, (2005) p. 77.
21. J. Peacey, X.J. Guo and E. Robles, *Proc. Vth Int. Conf. Copper 2003/Cobre 2003*, Santiago, Chile, (2003) p. 1.
22. I.J. Corrans and J.E. Angove, *Minerals Engineering*, 4 (1991) 763.
23. I.J. Corrans, G.D. Johnson and J.E. Angove, *Proc. XVIIIth Int. Miner. Process. Congress,* Sydney, (1993) p. 1227.
24. J.E. Angove, *Proc. Int. Conf. Randol Gold Forum,* Beaver Creek, Australia, (1993) p. 1-12.
25. I.J. Corrans and J.E. Angove, *Activation of mineral species*, Australian Patent 663 523, April 29, (1993).
26. I.J. Corrans, J.E. Angove and G.D. Johnson, *Proc. Int. Conf. Randol Gold Forum,* Perth, (1995) p. 221-224.
27. G.D. Johnson, H.A. Evans and J.H. Turner, *Proc. Int. Conf. ALTA 2000 Nickel/Cobalt-6*, Melbourne, Australia, (2000).
28. C.M. Palmer and G.D. Johnson, *Journal of Metals*, July (2005) 40.
29. H.E. Evans and G.D. Johnson, in *Copper Hydromet Roundtable ´99*, Randol International Phoenix, Arizona, (1999).
30. http://www.wmt.com.au
31. M. Adams and G.D. Johnson, *Proc. Int. Conf. ALTA 2001 Nickel/Cobalt-7*, Melbourne, Australia, (2001).
32. http://www.isamill.com
33. U. Enderle, P. Woodall, M. Duffy and N.W. Johnson, *Proc. XXth Int. Miner. Proc. Congr.,* (eds.) H. Hoberg, H. von Blattnitz, Aachen, Vol. 2, (1997) p. 71.
34. P. Baláž, F. Sekula, F. Jusko, M. Kočí, V. Dugas and L. Lauko, *Process for tetrahedrite ore treatment,* 1994, Slovak patent No. 081-94.
35. P. Baláž, *Extractive Metallurgy of Activated Minerals*, Elsevier, Amsterdam, (2000).
36. P. Baláž and M. Achimovičová, *Hydrometallurgy*, 84 (2006) 60.
37. R.A.D. Pattrick and A.J. Hall, *Mineralogical Magazine*, 47 (1983) 441.
38. C.G. Anderson and S.M. Nordwick, *Proc. EPD Congress,* (ed.) G.W. Warren, Anaheim, California, (1996) p. 323.
39. P. Baláž, F. Sekula, Š Jakabský and R. Kammel, *Minerals Engineering*, 8 (1995) 1299.
40. P. Baláž, R. Kammel, F. Sekula. and Š. Jakabský, *Proc. XXth Int. Miner. Proc. Congr.*, (eds.) H. Hoberg, H. von Blottnitz, Vol. 4, Aachen, (1997) p. 149.
41. F. Toda, *Organic Solid-State Reactions,* Kluwer, Amsterdam, (2002).
42. K. Tanaka, *Solvent-free Organic Synthesis,* Wiley-VCH, Weinheim, (2003).
43. G. Kaupp, *Organic Solid-State Reactions with 100% Yield.* Springer Berlin/Heidelberg, Vol. 254 in Book Series-Topics in Current Chemistry, (2005), p. 95-183.
44. D.E. Kaufmann, J.C. Namyslo, E. Gock and R. Florescu, *Verfahren zur Herstellung organischer Spurenelementverbindungen*, German patent, 2006, DE 10 2004 039 486 A1.
45. C. Suryanarayana, *Non-equilibrium Processing of Materials,* Pergamon Press, Oxford, (1999).
46. J.S. Benjamin, *Materials Science Forum*, 88-90 (1992) 1.
47. C. Suryanarayana, *Progress in Materials Science*, 46 (2001) 1.
48. K. Tkáčová, *Mechanical Activation of Minerals,* Elsevier, Amsterdam, (1989).
49. G. Heinicke, *Tribochemistry,* Academie-Verlag, Berlin, (1984).
50. E. Gock, *Mechanische Aktivierung von Phosporitkonzentraten im Hinblick auf den direkten Einsatz als Düngemittel*. Research report, Technical University Berlin, (1987), p. 35.
51. V. Yaneva, V. Petkova and D. Dombalov, *Chemistry for Sustainable Development*, , 13 (2005) 347.
52. M.V. Chaikina, *Chemistry for Sustainable Development*, 4 (1986) 71.
53. V.V. Boldyrev, N.Z. Lyakhov, M.V. Chaikina and M.G. Denisov, *Chemistry for Sustainable Development*, 4 (1996) 97.

54. J. Amgalan, M.V. Chaikina, M. Dulamsuren and A. Bilegbaatar, *Chemistry for Sustainable Development*, 6 (1998) 221.
55. C. Suryanarayana, *Mechanical Alloying and Milling,* Marcel Dekker, New York, (2004).
56. M. Bisrat and Ch. Nyström, *International Journal of Pharmaceutics*, 47 (1988) 223.
57. E. Merisko-Liversidge, in *Particles 2002*, Orlando, Florida, (2002) paper No. 45.
58. C.A. Lipinski, F. Lombardo, B.W. Domini and P.J. Freney, *Advanced Drug Delivery Reviews*, 23 (1997) 3.
59. L.X. Yu, G.L. Amidon, J.E. Polli, H. Zhao, M. Mehta, D.P. Conner, V.P. Shah, L.J. Lesko, M.L. Chen, V.H.L. Lee and A.S. Hussain, *Pharmaceutical Research*, 19 (2002) 921.
60. F.N. Bushrab and R.H. Müller, *New Drugs*, 5 (2003) 20.
61. J. Dutta. and H. Hoffmann, http://www.mxsg3.epfl.ch/ltp/Cours/Nanomat/pdf, 2003.
62. E.L. Parrott, *Journal of Pharmaceutical Sciences*, 63 (1974) 813.
63. E.L. Parrott, in *Encyclopedia of Pharmaceutical Technology*, (eds.) J. Swarbrick, J.C. Boylan. Vol. 3, Marcel Dekker, New York, (1990), p. 101.
64. A.V. Dushkin, *Chemistry for Sustainable Development*, 12 (2004) 251.
65. A.V. Dushkin, *Possibilities of mechanochemical technology in organic synthesis and enhancement of materials solubility*. DSc. Thesis, Novosibirsk, (2005) (in Russian).